CLAIMS

We claim:

- 1. A targeting construct comprising:
 - (a) a first polynucleotide sequence homologous to at least a first portion of an ACTHR gene;
 - (b) a second polynucleotide sequence homologous to at least a second portion of the ACTHR gene; and
 - (c) a selectable marker.
- 2. A method of producing a targeting construct, the method comprising:
 - (a) providing a first polynucleotide sequence homologous to at least a first portion of an ACTHR gene;
 - (b) providing a second polynucleotide sequence homologous to at least a second portion of the ACTHR gene;
 - (c) providing a selectable marker; and
 - (d) inserting the first sequence, second sequence, and selectable marker into a vector, to produce the targeting construct.
- 3. A cell comprising a disruption in an ACTHR gene.
- 4. The cell of claim 3, wherein the cell is a murine cell.
- 5. The cell of claim 4, wherein the murine cell is an embryonic stem cell.
- 6. A non-human transgenic animal comprising a disruption in an ACTHR gene.
- 7. The non-human transgenic animal of claim 6, wherein the transgenic animal is a mouse.
- 8. A cell derived from the transgenic mouse of claim 7.
- 9. A method of producing a transgenic mouse comprising a disruption in an ACTHR gene, the method comprising:
 - (a) introducing the targeting construct of claim 1 into a cell;
 - (b) introducing the cell into a blastocyst;
 - (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and
 - (d) breeding the chimeric mouse to produce the transgenic mouse.

- 10. A method of identifying an agent that modulates the expression or function of an ACTHR gene, the method comprising:
 - (a) providing a non-human transgenic animal comprising a disruption in an ACTHR gene;
 - (b) administering an agent to the non-human transgenic animal; and
 - (c) determining whether the expression or function of the disrupted ACTHR gene in the non-human transgenic animal is modulated.
- 11. A method of identifying an agent that modulates the expression or function of an ACTHR gene, the method comprising:
 - (a) providing a cell comprising a disruption in an ACTHR gene;
 - (b) contacting the cell with the agent; and
 - (c) determining whether the expression or function of the ACTHR gene is modulated.
- 12. The method of claim 11, wherein the cell is derived from the non-human transgenic animal of claim 6.
- 13. An agent identified by the method of claim 10 or claim 11.
- 14. A transgenic mouse comprising a disruption in an ACTHR gene, wherein there is no significant expression of the ACTHR gene in the transgenic mouse.
- 15. A transgenic mouse comprising a homozygous disruption in an ACTHR gene, wherein the transgenic mouse exhibits an adrenal gland abnormality.
- 16. The transgenic mouse of claim 15, wherein the adrenal gland abnormality comprises adrenal gland hypoplasia.
- 17. A transgenic mouse comprising a homozygous disruption in an ACTHR gene, wherein the transgenic mouse exhibits decreased cytoplasmic lipid vacuolation in brown adipose tissue, relative to a wild-type mouse.
- 18. A transgenic mouse comprising a disruption in an ACTHR gene, wherein the transgenic mouse exhibits an adipose tissue abnormality, relative to a wild-type mouse.
- 19. The transgenic mouse of claim 18, wherein the adipose tissue abnormality is characterized by reduced body fat percentage in the transgenic mouse, relative to a wild-type mouse.

- 20. A transgenic mouse comprising a homozygous disruption in an ACTHR gene, wherein the transgenic mouse exhibits a metabolic abnormality.
- 21. A transgenic mouse comprising a homozygous disruption in an ACTHR gene, wherein the transgenic mouse exhibits increased susceptibility to seizure.
- 22. The transgenic mouse of claim 21, wherein the mouse exhibits seizure-like responses at a lower dose of Metrazol, relative to a wild-type mouse.
- 23. A transgenic mouse comprising a homozygous disruption in an ACTHR gene, wherein the transgenic mouse exhibits increased activity relative to a wild-type mouse.
- 24. The transgenic mouse of claim 23, wherein the transgenic mouse is hyperactive.
- 25. The transgenic mouse of claim 24, wherein the hyperactivity is characterized by increased distance traveled in an open field test, relative to a wild-type mouse.
- 26. A transgenic mouse comprising a homozygous disruption in an ACTHR gene, wherein the transgenic mouse exhibits anti-depressive behavior, relative to a wild-type mouse.
- 27. The transgenic mouse of claim 26, wherein the transgenic mouse exhibits reduced time immobile when tail-suspended.
- 28. A cell derived from the transgenic mouse of claim 14.
- 29. A method of identifying an agent that ameliorates a phenotype associated with a disruption in an ACTHR gene, the method comprising:
 - (a) administering an agent to a transgenic mouse comprising a disruption in an ACTHR gene; and
 - (b) determining whether the agent ameliorates at least one of the following phenotypes: an adrenal gland abnormality, an adipose tissue abnormality, a metabolic abnormality, increased activity, anti-depressive behavior, or increased susceptibility to seizure.
- 30. An agent identified by the method of claim 29
- 31. A method of treating susceptibility to seizure, the method comprising administering to a subject in need a therapeutically effective amount of ACTHR.
- 32. A method of treating hyperactivity, the method comprising administering to a subject in need a therapeutically effective amount of ACTHR.

- 33. A pharmaceutical composition comprising an ACTHR protein.
- 34. A method of identifying an agent that ameliorates susceptibility to seizure, the method comprising:
 - (a) administering a putative agent to the transgenic mouse of claim 21; and
 - (b) determining whether the agent has an affect on susceptibility to seizure in the transgenic mouse.
- 35. A method of identifying an agent that ameliorates hyperactivity, the method comprising:
 - (a) administering a putative agent to the transgenic mouse of claim 23; and
 - (b) determining whether the agent has an affect on hyperactivity in the transgenic mouse.
- 36. A method of identifying an agent that inhibits the activity or function of ACTHR, the method comprising:
 - (a) providing a cell expressing ACTHR;
 - (b) contacting the cell with an agent; and
 - (c) determining whether the agent inhibits the activity or function of ACTHR, wherein the agent has an affect on depression.
- 37. An agonist or antagonist of ACTHR.
- 38. Phenotypic data associated with a transgenic mouse comprising a disruption in an ACTHR gene, wherein the phenotypic data is in an electronic database.